REMARKS/ARGUMENTS

Claims 1-9 and 13-23 remain in this application. Review and reconsideration on the merits are respectfully requested in view of the following comments.

Claims 1-6, 8-9 and 13-23 stand rejected as being unpatentable over Rampal et al. (WO 03/017981). Applicants note that the Office action refers to the claims as being directed to "an extended release tablet comprised of a macrolide antibiotic, water-soluble excipients, and a binder." See Office action, page 3. However, as noted in previous the response, the claims have been amended to use the transitional phrase "consisting essentially of" with respect to the composition of the extended release tablet. Accordingly, the use of the partially close transitional phrase limits the extended release tablet to materials listed and any other materials that do not affect the basic and novel characteristics of the invention. Applicants respectfully submit that when the claims are construed taking into consideration the transitional phrase "consisting essentially of," the claims of the present application clearly distinguish over and are, therefore, patentable over the cited references.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established. To establish a *prima facie* case of obviousness, there must be some motivation or suggestion in the references that would lead one of ordinary skill in the art to modify the reference or combine the various components, without knowledge of the claimed invention, to obtain the present invention. *In re Kotzab,* 217 F. 3d 1365, 1371, 55 U.S.P.Q. 2d (BNA) 1313, 1317 (Fed. Cir. 2000) ("particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed"). The mere identification of the various components in the prior art references is insufficient to render the present invention obvious. The motivation or suggestion "must be considered in the context of the teaching of the entire reference." *Id.* Rampal fails to disclose or suggest a dosage form that does not contain high viscosity, rate controlling polymers to control release. Furthermore, as acknowledged in the Office action, Rampal fails to disclose or suggest the use of low viscosity HPC or HPMC. The Office has taken the position that the

necessary motivation or suggestion is present because "(1) Rampel et al. disclose a controlled and extended release formulation; (2) a wide variety of cellulosic ether polymers are commercially available with various viscosity grades that are known for controlled release formulation; and (3) hydroxypropylcellulose polymers under the trade name, Klucel®, has been disclosed, which possesses an average viscosity between 3 to 15 cps." Applicants submit that Rampal is devoid of any suggestion of utilizing low viscosity binder polymer as set forth in the pending claims. One of skill in the art would never arrive at the present invention based on Rampal without the benefit of the applicants' disclosure. Although a reference need not expressly teach that the disclosure contained therein should be modified, the modification must nevertheless be "clear and particular." *Winner Inter. Royalty Corp. v. Wang,* 202 F. 3d 1340, 1348-1349 (Fed. Cir. 2000). Certainly, there is nothing disclosed in Rampal that provides "clear and particular" motivation to one of ordinary skill in the art to utilize low viscosity binder in the absence of conventional rate controlling (high viscosity) polymers.

While Rampal does disclose that a wide variety of cellulosic ether polymers are commercially available, the reference only teaches the use of high viscosity rate controlling polymers to provide extended release. The high viscosity rate controlling polymers are essential to the Rampal formulation and a fair reading of the document in its entirety clearly demonstrates that the controlled release tablet formulations are dependent upon the rate controlling polymers for controlling drug release. The abstract and the field of the invention sections of Rampal both refer to using "one or more of rate controlling cellulosic ether polymers." Furthermore, the background section repeatedly refers to the use of high viscosity cellulosic ether polymers as rate controlling polymers in the formulation. Although Rampal acknowledges the simple fact that these polymers are commercially available in different viscosity grades, there is no indication or suggestion that all viscosity grades are capable of performing as rate controlling polymers in the formulation. In fact, the clear teaching of the reference is exactly the opposite. Only certain high viscosity polymers are described as being acceptable to provide controlled drug release in the tablet formulations. Examples 1-5 and 7-8 all disclose the use of two grades of high viscosity, (4,000 cps and 15,000 cps) rate controlling hydroxypropylmethylcellulose as rate controlling polymers. Furthermore, the reference fails to provide any teaching or suggestion that the lower viscosity polymers (3 to 15 cps) set forth in the claims of the present application would

ever be used as rate controlling polymers in the controlled release formulations. To the contrary, Rampal teaches away from the use of low viscosity polymers by the constant reference to and limited disclosure to high viscosity grades. Therefore, applicants respectfully submit that Rampal not only fails to suggest using the low viscosity grades but explicitly teaches away from such usage.

The Office action further indicates that hydroxypropylmethylcellulose polymers under the trade name Klucel® have been disclosed that possess an average viscosity between 3 and 15 cps. As with the other polymers, Klucel® refers to a family of polymers rather than a single specific polymer. The various grades have different molecular weights and viscosities and, therefore, serve different purposes. Below is a table from the manufacturer of Klucel®, Aqualon, describing the various grades of Klucel® and the corresponding viscosities and molecular weights.

KLUCEL® HPC PHARM Grade	Aqueous Solution Viscosity: Typical Brookfield at Concentration Shown, mPas	Molecular Weight (weight averaged)
HF	1,500-3,000 at 1%	1,150,000
MF	4,000-6,500 at 2%	850,000
GF	150-400 at 2%	370,000
JF	150-400 at 5%	140,000
LF	75-150 at 5%	95,000
EF	300-600 at 10%	80,000

Applicants note that the present application refers to the use of Klucel® LF, which is a low viscosity grade polymer and not a rate controlling polymer. Rampal's statement that a wide range of viscosity grades of HPC are available under the trade name Klucel®, fails to provide any teaching or motivation that would lead one of ordinary skill in the art to the use of a low

viscosity grade as set forth in the claims of the pending application. For at least this reason, applicants respectfully submit that the claims of the pending application are non-obvious over Rampal et al. and request that the rejection be withdrawn.

Claim 7 stand rejected as being unpatentable over Rampal et al. in view of Vanderbist et al. (WO 02/24174). According to the Office action, however, Vanderbist fails to remedy the shortcomings of Rampal because there is no motivation or suggestion to prepare a dosage form using low viscosity binders in the absence of rate controlling polymers. Furthermore, Rampal and Vanderbist even when combined fail to render obvious claim 7 of the pending application, which refers to microcrystalline cellulose at a concentration of about 1-4% by weight. Vanderbist discloses the use of 5-50% by weight microcrystalline cellulose, which is outside the claimed range.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness as the cited reference has failed to disclose each and every limitation of the claims and, furthermore, even when combined the references fail to disclose the present invention. For at least this reason as well, applicants respectfully request that the rejection be withdrawn.

In view of the foregoing, it is respectfully submitted that all of the pending claims are in condition for allowance and favorable action on the merits is requested. Any questions concerning this application may be directed to applicant's undersigned attorney at the telephone number indicated below. The Commissioner is authorized to charge any additional fees required or to credit any overpayment to Deposit Account No. 20-0809.

Respectfully submitted,

/John F. Kane/
John F. Kane, Reg. No. 44,815

THOMPSON HINE LLP
2000 Courthouse Plaza NE
10 West Second Street
Dayton, Ohio 45402-1758
(937) 443-6816